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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/765,491	01/18/2001	Jack L. Arbiser	EU 98055 CON	8772

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EXAMINER	
KIM, JENNIFER M	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 03/31/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/765,491	ARBISER, JACK L.	
	Examiner	Art Unit	
	Jennifer Kim	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 October 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4-6,10-12 and 17-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-6,10-12 and 17-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed October 4, 2004 have been received and entered into the application.

Action Summary

The rejection of claims 4-6 and 17-19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of the specific "angiogenesis inhibitor", does not reasonable provide enablement for the terms "collagenase inhibitors, angiogenic fumagillin derivatives, 2,5-diaryltetrahydrofurans, aminophenylphosphonic acid compounds, 3-substituted oxindole derivatives, tetracyclines inhibiting collagenase and a sulfated polysaccharides" is hereby expressly withdrawn in view of Applicant's persuasive argument. However, the rejection of claims 4-6 and 17-19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, not reasonable provide enablement for the "**effective amounts**" of "collagenase inhibitors, angiogenic fumagillin derivatives, 2,5-diaryltetrahydrofurans, aminophenylphosphonic acid compounds, 3-substituted oxindole derivatives, tetracyclines inhibiting collagenase and a sulfated polysaccharides" is maintained for the reasons set forth in previous Office Action.

The rejection of claims 4-6, 10-12 18, and 19 rejected under 35 U.S.C. 112 second paragraph, for the term "symptoms" in claims 4 and 10 as being vague and indefinite is withdrawn in view of Applicant's persuasive argument.

The rejection of claims 4-6 and 17 rejected under 35 U.S.C. 112 second paragraph for the term "effective amount" as being indefinite is maintained for the reasons stated in the previous office action.

The rejection of claims 10-12 and 18 under 35 U.S.C. 102(e) as being anticipated by Aggarwal (WO 95/18606) of record evidenced by Doland's Medical Dictionary (1994) of record is hereby expressly withdrawn in view of Applicant's amendment.

The rejection of claim 17 under 35 U.S.C. 102(e) as being anticipated by Golub et al. (U.S.Patent No. 6,015,804) is hereby expressly withdrawn in view of Applicant's amendment.

The rejection of claims 4 and 5 under 35 U.S.C. 103(a) as being unpatentable over O'Reilly et al. (U.S.Patent No. 5,733,876) of record in view of Brem et al. (U.S. Patent No. 6,482,810B1) and further in view of Doland's Illustrated Medical Dictionary, 1994 of record is hereby expressly withdrawn in view of Applicant's amendment.

The rejection of claims 4 and 5 under 35 U.S.C. 103(a) as being unpatentable over O'Reilly et al. (U.S.Patent No. 5,733,876) of record in view of Andrulis Jr. et al. (U.S. Patent No. 5654312) of record and further in view of Doland's Illustrated Medical Dictionary, 1994 of record is hereby expressly withdrawn in view of Applicant's amendment.

The rejection of claims 4-6 under 35 U.S.C. 103(a) as being unpatentable over O'Reilly et al. (U.S.Patent No. 5,733,876) of record in view of Teicher et al. (U.S.Patent No. 5,776,898) and further in view of Doland's Illustrated Medical Dictionary, 1994 of record is hereby expressly withdrawn in view of Applicant's amendment.

The rejection of claim 17 under 35 U.S.C. 103(a) as being unpatentable over O'Reilly et al. (U.S.Patent No. 5,733,876) of record in view of Tanaka et al. (U.S.Patent No. 4,900,815) and Brem et al. (U.S.Patent No. 6,482,810B1) and further in view of Doland's Illustrated Medical Dictionary(1994) of record is hereby expressly withdrawn in view of Applicant's amendment.

The rejection of claims 10-12 under 35 U.S.C. 103(a) as being unpatentable over Galardy (U.S.Patent No. 5,696,147) of record and Arbiser et al. (June, 1999) of record in view of Thaloor et al. (1998) of record is hereby expressly withdrawn in view of Applicant's amendment.

The rejection of claims 10-12 and 19 under 35 U.S.C. 103(a) as being unpatentable over Arbiser et al. (June, 1999) of record in view of Thaloor et al. (1998) of record is hereby expressly withdrawn in view of Applicant's amendment.

Applicant's amendment necessitated additional rejections presented in this Office action.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claim 17 is rejected under 35 U.S.C. 102(e) as being anticipated by Wirostko (U.S.Patent No. 6,218,368 B1).

Wirostko teach teatracyclines are known to have "collagenase inhibition properties and used chronically as therapy for diverse diseases including acne rosacea. (column 2, lines 13-30).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and

> the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 4 and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Deutch et al. (U.S.Patent No. 5,190,918) in view of Brem et al. (U.S.Patent No. 6,482,801B1) of record.

Deutch et al. teach angiogenesis activity is defined as the ability to enhance the formation of lymph vessels (lymphangiogenesis). (column 3, lines 20-25).

Deutch et al. do not teach the collagenase inhibitors for the treatment of formation of lymph vessels (lymphangiogenesis).

Brem et al. teach tetracyclines inhibiting collagenase such as minocycline is effective inhibitors of angiogenesis. (column 3, lines 43-46 and column 2, lines 60-64).

It would have been obvious to one of ordinary skill in the art to employ collagenase inhibitors including minocycline for the treatment of lymphangiogenesis because lymphangiogenesis involves angiogenesis activity of forming a blood vessels as taught by Brem et al. One would have been motivated to employ collagenase inhibitor (e.g. minocycline) with a reasonable expectation of successfully treating formation of lymph vessels (lymphangiogenesis) with a reasonable expectation of successfully treating the disease mediated by angiogenesis.

Claims 4 and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Deutch et al. (U.S.Patent No. 5,190,918) in view of Andrulis Jr. et al. (U.S.Patent No. 5654312) of record.

Deutch et al. teach angiogenesis activity is defined as the ability to enhance the formation of lymph vessels (lymphangiogenesis). (column 3, lines 20-25).

Deutch et al. do not teach thalidomide for the treatment of formation of lymph vessels (lymphangiogenesis).

Andrulis Jr. et al. teach that thalidomides are effective angiogenesis inhibitor. (abstract, column 1, lines 47-48, lines 55-56). Andrulis Jr. et al. teach thalidomides maybe administered topically (column 4, lines 55-60, and column 6, line 18, line 43 and line 57).

It would have been obvious to one of ordinary skill in the art to employ thalidomide for the treatment of lymphangiogenesis because lymphangiogenesis is which is formation of lymph vessels is caused by angiogenesis as taught by Deutch et al. and because thalidomides are effective angiogenesis inhibitor as taught by Andrulis Jr. et al. One would have been motivated to employ thalidomide with a reasonable expectation of successfully treating a diseased mediated by angiogenesis in order to achieve effective angiogenesis inhibition of thalidomide.

Claims 4-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Deutch et al. (U.S.Patent No. 5,190,918) in view of Teicher et al. (U.S.Patent No. 5,776,898) of record.

Deutch et al. teach angiogenesis activity is defined as the ability to enhance the formation of lymph vessels (lymphangiogenesis). (column 3, lines 20-25).

Deutch et al. do not teach angiogenic fumagillin derivatives such as TNP-470 for the treatment of formation of lymph vessels (lymphangiogenesis).

Teicher et al. teach that TNP-470 is an antiangiogenic agent. (column 7, lines 40-41, column 17, lines 40-50).

It would have been obvious to one of ordinary skill in the art to employ angiogenic fumagillin derivatives such as TNP-470 for the treatment of lymphangiogenesis because lymphangiogenesis is caused by angiogenesis involving formation of lymph vessels and because TNP-470 is an angiogenesis inhibitor as taught by Teicher et al. One would have been motivate do employ TNP-470 with a reasonable expectation of successfully treating a disease mediated by angiogenesis (formation of lymph vessel e.g. lymphangiogenesis) in order to achieve effective angiogenesis inhibition of TNP-470 as taught by Teicher et al.

Claims 10-12 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Aggarwal (WO 95/18606) of record.

Aggarwal teach method for the treatment of melanomas (malignant melanoma), basal cell carcinoma, squamous cell carcinoma, soft tissue sarcomas, comprising administration of effective dose of curcumin (mixture of demethoxycurcumin). (page 5, lies 20-32, page 6). Aggarwal teach the composition comprising curcumin can be formulated topical in ointment form. (page, 7, lines 26-28, page 8, lines 7-15). Aggarwal teach the effective dose of curcumin and curcumin analogues are administered in a dose of from about 1 microgram to about 100milligram. (page 6, lines 6-11).

Aggarwal does not expressly teach the specific formulation set forth in claim 10.

It would have been obvious to one of ordinary skill in the art to modify the composition taught by Aggarwal in topical ointment formulation with effective range of curcumin for the treatment of malignant melanoma, basal cell carcinoma, squamous cell carcinoma, soft tissue sarcomas because Aggarwal teach curcumin composition can be formulated in topical ointment formulation with effective amount about 1 microgram to about 100milligrams and because Aggarwal teach curcumin is useful for the treatment of malignant melanoma, basal cell carcinoma, squamous cell carcinoma, soft tissue sarcomas. One would have been motivated to make such a modification in order to successfully treating malignant melanoma with topical curcumin formulation taught by Aggarwal.

Claims 10-12 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Arbiser et al. (June, 1999) of record in view of Thaloor et al. (1998) of record and further in view of Aggarwal (WO 95/18606) of record.

Arbiser et al. on the abstract, teach that patients with recessive dystrophic epidermolysis bullosa (RDEB) are suggested to treat with angiogenesis inhibitors. Arbiser et al. also teach that the patients with RDEB have elevated levels of basic fibroblast growth factor (bFGF) and that angiogenesis inhibitors may antagonize the effects of bFGF. Arbiser et al. teach that there are currently no other means of treatment of the disorder, which has a nigh morbidity and mortality rate.

Arbiser et al. lack curcumin and demethoxycurcumin and specific formulation set forth in claim 10.

Thaloor et al. teach that curcumin inhibits angiogenesis. (abstract).

Aggarwal teach the composition comprising curcumin can be formulated topical in ointment form. (page, 7, lines 26-28, page 8, lines 7-15). Aggarwal teach the effective dose of curcumin and curcumin analogues are administered in a dose of from about 1 microgram to about 100milligram. (page 6, lines 6-11).

It would have been obvious to one of ordinary skill in the art to employ curcumin or curcuminoids (ie.demethoxycurcumin) for the treatment of RDEB with topical formulation of curcumin taught by Aggarwal in the angiogenesis effective amounts because Arbiser et al. suggested that angiogenesis inhibitors are effective in treatment of RDEB and because curcumin or curcuminoids possess angiogenesis inhibiting property as taught by Thaloor et al. Further, curcumin or curcuminoids can be formulated in ointment formulation with wide range of dose form about 1 microgram to about 100milligrams as taught by Aggarwal. One would have been motivated to formulate curcumin for curcuminoids in topical formulation with angiogenesis effective amounts for the treatment of RDEB in order to avoid death of a patient with RDEB with only available angiogenesis inhibition treatment taught by Arbiser et al.

For these reasons the claimed subject matter is deemed to fail to patentably distinguish over the state of the art as represented by the cited references. The claims are therefore properly rejected under 35 U.S.C. 103.

Response to Arguments

Applicant's arguments filed October 4, 2004 have been fully considered but they are not persuasive. Applicant argues that one of ordinary skill in the art could routinely arrive at an effective amount of the drugs and method of delivery to treat the claimed disorders and the term "effective amounts" is a common generally acceptable term for pharmaceutical claims and is not ambiguous or indefinite, provided that a person of ordinary skill in the art could determine the specific amounts without undue experimentation, as is the case here. This is not persuasive because there is a plethora of active agents and, therefore, it would be undue experimentation to determine effective amounts for every active agent. It is noted that these active agents do not possess common moiety and differ in physical and chemical characteristics; one range may not cover all the active agents. Further, one of ordinary skill in the art reading the claim could not determine its metes and bounds regarding effective amounts because there is no such range provided or defined in the specification.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

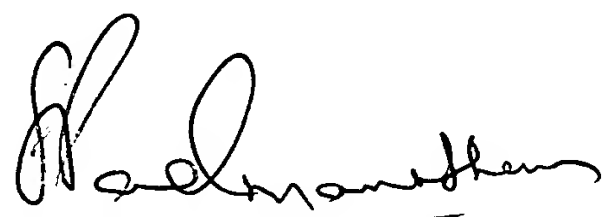
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Kim whose telephone number is 571-272-0628. The examiner can normally be reached on Monday through Friday 6:30 am to 3 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Sreenivasan Padmanabhan

Supervisory Examiner
Art Unit 1617

Jmk
March 18, 2005